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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/356,322	11/24/1998	TIDHAR DARI SHALON	STFD:009--1	7679

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EXAMINER	
MARSCHEL, ARDIN H	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/18/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/356,322	Brown et al.
Examiner	**Art Unit**
Ardin Marschel	1631

-- The MAILING DATE of this c mmunication appears on th cov r sh et with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Sep 26, 2001

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 7-39 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 7-39 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) ~~Paper No(s).~~ 2 sheets

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☒ Other: Attachment for PTO-948

Applicants' arguments, filed 9/26/01, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because two sequences are present on page 41 of the instant application which do not have SEQ ID NOs amended to accompany the sequences. Thus, applicants are required to amend SEQ ID NOs. into the specification at the page 41 sequences. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

Applicants are hereby notified that the required timing for the correction of drawings has changed. See the last 6 lines on the sheet which is attached entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". It is noted that a PTO Form 948 was mailed with Paper No. 6 on 6/20/00. Due to the above

notification Applicant is required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

Claims 7-35, 38, and 39 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims contain NEW MATTER as previously summarized in the office action, mailed 3/26/01, which noted that it was revealed that written basis for the generic phrase "each region of the microarray is free of cross-contamination with..." is NEW MATTER. This rejection is reiterated below and maintained from the previous office action, mailed 3/26/01. Applicants argue that a preliminary amendment was filed with the filing of the instant application directed to the above noted subject matter. It, however, is noted that the instant application was filed as a continuation of the parent serial number 08/688,488 and not as a continuation-in-part. No reference to this amendment has been made nor has the filing status been changed by applicants to a continuation-in-part. Thus, these limitations

fall under the conditions cited in the MPEP at § 608.04(a) as being NEW MATTER and not 608.04(b). Therefore, the argument that the preliminary amendment is not NEW MATTER is not persuasive on the above argued grounds. Applicants argue further that the above indicated limitation is inherent in their previous parent etc. disclosures via the disclosure of individually depositing desired DNA at each region of a microarray. In response this is non-persuasive because such deposition disclosure lacks any consideration or mention of cross contamination, or its extent, if it is present. Thus, whether deposition of DNA is free of cross contamination, or, alternatively, may result in some cross contamination, such as an insignificant amount, or, alternatively, significant cross contamination is completely lacking is such a deposition disclosure, thus supporting this NEW MATTER rejection.

Firstly, written description of the above phrase as filed in the instant application has not been found. Secondly, the control of cross-contamination has only been described in previous applications via the particular method of capillary dispensing with tapping on the solid support of the DNA sequences to form the microarrays of the instant invention. This is emphasized in the claims of parent U.S. Patent 5,807,522. It is also summarized in the instant specification in the bridging paragraph between pages 11 and 12. These are not generic

regarding the prevention of cross-contamination as now claimed.

It is also noted that NEW MATTER is present in claim 21 in that both the generic 400 or more regions has not been found as filed other than also connected to a 2,500 region/cm^2 density; although claim 23 does, as a single claim, have this 2,500 regions/cm^2 density. Also, the densities in said claim 21 of "about 62,500 regions/cm^2 and about 625 regions/cm^2 have not been found as filed. Thus claim 21 and those dependent therefrom also contain NEW MATTER. Applicants argue regarding a "step(b)" regarding "400 or more regions" and the density limitations. No such step (b) has been found. Applicants are requested to submit evidence of where this "step(b)" is present as to written description. Applicants then argue that the densities flow directly from the 0.002 and 2 nl drop sizes which result in 20 - 200 micrometer region diameters. This is an allegation without factual support because the region diameter formed from a drop depends on several parameters, not the least of which are the drop liquid viscosity and the wettability of the substrate surface onto which the drop is deposited. This is not seen as to how these drop sizes support the above noted NEW MATTER densities. This rejection is reiterated above and maintained from the previous office action, mailed 3/26/01.

PRIORITY FOR THE INSTANT CLAIMS:

Applicants have argued that the priority date should be

granted earlier than that determined below due to the lack of claims 36 and 37 being included in the above NEW MATTER rejection. In response the priority date is determined by the date of disclosure of a claim and not whether it contains NEW MATTER or not. Thus the below priority determination is reiterated and repeated as still proper as applicants have not supplied evidence to the contrary.

The priority date for the instant claims has been considered and such consideration reveals that the earliest priority date for all of the instantly pending claims is that of the filing date of the immediate parent application, Serial Number 08/688,488; which is July 30, 1996. This earliest priority date is based on a lack of written description of certain limitations which are present in all of the instant claims either directly or via dependence from an independent claim. It is noted, for example, that the generic limitation in instant claim 7 directed to 400 or more regions is not correspondingly limited as to the region density for an array which contains 400 or more regions. Consideration of the previous parent application, for example, Serial Number 08/514,875 therein at page 21, lines 4-6, reveals that a 400 region array is described but also on a 16 mm^2 array for a density of 2,500 regions/cm^2. A generic 400 region array as now claimed in instant claims 7, 21, 34, 36, and claims dependent therefrom is thus not described in said parent

application. Similarly, the densities of "about 62,500 and about 625 regions/cm^2 as present in instant claim 21 has not been found in said parent application. A review of earlier parent applications also failed to reveal written support for the above limitations. Another limitation that has not been found in the parent application prior to said July 30, 1996, is the generic limitation of regions in the microarray which are "free of cross-contamination..." without also requiring that this is achieved in a particular way. This particular way of preventing cross-contamination is via a capillary dispensing methodology with the tapping of the dispensing capillary on the solid support during deposition as claimed, for example, in the U.S. Patent 5,807,522 which matured from a parent application compared to the instant application. It is noted that the instant claims are generic regarding this cross-contamination prevention and are not limited as to what is performed to achieve it as in the claims of said U.S. Patent 5,807,522. Thus, in summary, the priority date for the presently instantly pending claims is only granted to July 30, 1996.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an

> application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 7-20 and 34-39 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Lipshutz et al.(P/N 6,013,440).

This rejection is reiterated below and maintained from the previous office action, mailed 3/26/01, as the above priority determination argued by applicants has not been changed thus leaving this rejection still deemed proper.

In the abstract, lines 1-5, and in column 2, lines 9-15, Lipshutz et al. describes affinity matrices which "bear a large number of different nucleic acid affinity ligands". In column 5, lines 1-3, the affinity matrix is described as having at least one oligonucleotide that is complementary to each known expressed RNA in a sample which is deemed to describe the presence of unique oligonucleotide type polynucleotides on said matrix. Sample sequences are disclosed in column 6, line 66, through column 7, line 8, as being present absent, or in an amount which is clearly inclusive of the quantities as described in instant claims 35, 38, and 39. DNA probes as present on the matrix is disclosed in column 6, lines 60-65. In column 5, lines 25-46, the single stranded oligonucleotides on said matrix, or solid support, clearly include lengths up to 1000 nucleotides with

specific lengths given as greater than 50, 150, 250, and 500 nucleotides thereon as species of such lengths. The affinity matrices as summarized in column 5, lines 42-67, are deemed to be the solid supports as instantly claimed, or alternatively referred to as microarrays in the instant claims and include surface moieties such as aldehyde, in polyformaldehyde, or carboxyl, in an acetate surface, as also required in instant claim 13. The formation of matrices via various synthetic methods, both chemical and enzymatic, is summarized in column 10, lines 13-65, and in column 16, line 47, through column 21, line 33, wherein column 10, lines 24-26, specifically describe the presence of polynucleotide composition spots. Each spot is separately formed with a different oligonucleotide thereon. Spot density species and numbers of spots per array are disclosed in the reference in column 16, lines 58-66. The arrays may be made up of glass etc. as summarized in column 5, lines 42-67. Spotting preparatory methodology is set forth in column 18, lines 24, through column 19, line 45, as including micropipettes, tubes etc. Hydrophobic coating on the array surface is disclosed in column 19, lines 16-24, (regarding instant claim 12) as well as the prevention of cross-contamination via these coatings. These synthetic methods as are known in the art and summarized as such in column 20, lines 3-25 result in covalent immobilization of nucleic acids as required in instant claim 14. The formation of

probes via amplification to result in non-covalently linked oligonucleotides as required in instant claim 15 is described in the reference in column 22, lines 1-10. Streptavidin on the support, as disclosed in column 23, lines 52-58, may be utilized which contains multiple cations and thus qualifies as a polycationic polymer regarding instant claim 16. These disclosures are deemed to anticipate the above listed instant claims.

Claims 7, 11-15, 17, 18, 20, and 34 are rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Dehlinger(P/N 5,723,320).

This rejection is reiterated below and maintained from the previous office action, mailed 3/26/01, as the above priority determination argued by applicants has not been changed thus leaving this rejection still deemed proper.

Dehlinger describes the usefulness of utilizing hybridization probe arrays for detection and analysis of gene expression and diagnostics for a desired disease condition or desired biological function for genes of interest as summarized in column 1, lines 38-43, and in column 13, line 54, through column 14, line 18. The remainder of the disclosure of Dehlinger is directed to methods of making such arrays including describing several options for the immobilized probes thereon. One option for the templates for the formation of arrays is given in column

13, lines 8-10, as ESTs. In column 13, lines 21-50, these templates are hybridized to a recognition sequence and then subjected to polymerase extension. The templates are then removed leaving regions on the array with "different-sequence" gene probes in each region up to several hundred bases in length. The uniqueness of the probes on the array of the reference is emphasized in column 2, lines 49-67, where the probes are not only described as being unique but also each having a "different-sequence". The array density of polynucleotide probes of the reference is generally high with a preference at $1000/cm^2$ as given in column 3, lines 17-22, and column 5, lines 31-35, but not disclosed as limited only to those densities. High numbers of DNA sequences on the array of the reference include numbers such as 4096 set forth in column 6, lines 28-31, but without indicating that this exemplified number is limiting. Another option for array preparation is to covalently couple oligomers to filaments made up of metal wire as summarized in column 5, line 53, through column 7, line 27, wherein the crosslinking of oligomers to a polymer coating occurs via irradiation. Such metal wires are inherently non-porous and hydrophobic as required in instant claims 11 and 12. These surfaces contain amines as in polyacrylamide as required in instant claim 13 and an option. They may be synthesized in monomer addition steps as set forth in column 7, line 35, through column 8, line 24, which is via

hydroxyl groups as also required in instant claim 13. Hybridization of complementary target sequences as given in column 13, lines 21-67, also anticipates instant claim 15. These disclosures anticipate the above instant claims.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 21-33 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lipshutz et al.(P/N 6,013,440).

This rejection is reiterated below and maintained from the previous office action, mailed 3/26/01, as the above priority determination argued by applicants has not been changed thus leaving this rejection still deemed proper.

The above description of Lipshutz et al. indicates that the reference describes the essentials of the microarrays as instantly claimed as are set forth in claims dependent from instant claim 21. It is noted that several methods of making the arrays are described in Lipshutz et al. including a method of spotting as well as utilizing micropipettes as summarized in column 19, lines 25-45. These synthetic methods are preceded by the suggestion in column 16, lines 58-66, that spot densities of 400,000 probes per cm^2 are possible. An estimated calculation from this density reveals that this density corresponds to an approximate spot size having a radius of 0.75×10^{-3} cm which, if calculated for a droplet of this radius would give a 2 nanoliter droplet which corresponds to the 2 nl volume required in instant claim 21. It is also noted that the densities in the reference cover a range of 60 to 400,000 probes per cm^2 which includes the species of densities of instant claim 21.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to prepare the high density arrays of the reference which are suggested to include a high enough density that spotting methods in the

reference would be utilized with solution amounts as required in instant claim 21 thus resulting in the invention of claims 21 etc. with a reasonable expectation of success.

On the enclosed PTO Form 1449, filed 5/22/01, several citations are lined through due to a lack of a date of publication which is required for any citation of a PTO Form 1449.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 14, 2001

ARDIN H. MARSCHEL
PRIMARY EXAMINER

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.